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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/701,550	11/05/2003	Theo T. Nikiforov	100/07934	1067
21569	7590	09/14/2006		
CALIPER LIFE SCIENCES, INC. 605 FAIRCHILD DRIVE MOUNTAIN VIEW, CA 94043-2234			EXAMINER CALAMITA, HEATHER	
			ART UNIT	PAPER NUMBER
			1637	

DATE MAILED: 09/14/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

Application No.

10/701,550

Applicant(s)

NIKIFOROV, THEO T.

Examiner

Heather G. Calamita, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 12 June 2006.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-28 is/are pending in the application.
- 4a) Of the above claim(s) 10-16 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-9 and 17-28 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_.
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

**DETAILED ACTION***Status of Application, Amendments, and/or Claims*

1. Amendments of June 12, 2006, have been received and entered in full. Claims 1-28 are pending. Claims 1-9 and 17-28 are under examination. Claims 10-16 are withdrawn as being directed to non-elected subject matter. This action is made NON-FINAL. Any objections and rejections not reiterated below are hereby withdrawn.

*Double Patenting*

2. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-9 and 17-28 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-10 of U.S. Patent No. 6,699,655. Although the conflicting claims are not identical, they are not patentably distinct from each other because Claim 1 is generic to claims 1-10 of U. S. Patent NO. 6,699,655. That is, claims 1-10 of U. S. Patent NO. 6,699,655 fall entirely within the scope of claim 1 of the instant application, or in other words, claim 1 is anticipated by claims 1-10 of U. S. Patent NO. 6,699,655. Specifically,

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claim 1 of the instant application is drawn to a method of measuring the activity of a kinase enzyme comprising:

a) providing a fluorescently labeled phosphorylatable compound, a kinase enzyme and a phosphate donor group where the kinase enzyme transfers the phosphate group from the phosphate donor group to the phosphorylatable compound to make a phosphorylated product,

b) contacting the phosphorylated product with a protein having a chelating group associated therewith, and a multivalent metal ion chelated by the chelating group, and determining a level of phosphorylated product by detecting a level of fluorescence intensity emitted from the reaction mixture.

Claims 1-10 of US Patent 6,699,655 are drawn to a method of determining whether a compound is phosphorylated, the compound comprising a fluorescent label, the method comprising: contacting the compound with a kinase enzyme in the presence of a phosphate donor group and providing the compound in a mixture with a binding component, wherein the binding component comprises multivalent metal ions and is sufficiently large to induce a shift in an amount of polarized fluorescence emitted from the compound, when the binding component binds the compound; and detecting whether the binding component binds to the compound by monitoring the amount of polarized fluorescence emitted from the mixture, binding of the binding component to the compound being indicative that the compound is phosphorylated.

The claims of the US Patent 6,699,655 are species of the instant claims.

3. Claims 1-9 and 17-28 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 18-36 of U.S. Patent No. 6,472,141. Although the conflicting claims are not identical, they are not patentably distinct from each other because Claim 1 is generic to claims 18-36 of U.S. Patent No. 6,472,141. That is, claims 18-36 of U.S.

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Patent No. 6,472,141 fall entirely within the scope of claim 1 of the instant application, or in other words, claim 1 is anticipated by claims 18-36 of U.S. Patent No. 6,472,141. Specifically, claim 1 of the instant application is drawn to a method of measuring the activity of a kinase enzyme comprising:

a) providing a fluorescently labeled phosphorylatable compound, a kinase enzyme and a phosphate donor group where the kinase enzyme transfers the phosphate group from the phosphate donor group to the phosphorylatable compound to make a phosphorylated product,

b) contacting the phosphorylated product with a protein having a chelating group associated therewith, and a multivalent metal ion chelated by the chelating group, and determining a level of phosphorylated product by detecting a level of fluorescence intensity emitted from the reaction mixture.

Claim 18 of US Patent 6,472,141 is drawn to a method of monitoring the activity of a kinase enzyme, comprising: providing a first mixture comprising a phosphorylatable compound that includes a fluorescent label, a kinase enzyme and a phosphate donor group, wherein the kinase enzyme is capable of phosphorylating the phosphorylatable compound to produce a phosphorylated product; contacting the phosphorylated product with a polycationic component; and monitoring a level of phosphorylated product produced by the activity of the kinase enzyme by monitoring binding of the polycationic component to the phosphorylated product.

The claims of the US Patent 6,472,141 are species of the instant claims.

4. Claims 1-9 and 17-28 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 40 of US Patent 6287,774. Although the conflicting claims are not identical, they are not patentably distinct from each other because Claim 1 is generic to claim 40 of US Patent 6287,774. That is, claim 40 of US Patent 6287,774 falls entirely

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within the scope of claim 1 of the instant application, or in other words, claim 1 is anticipated by claim 40 of US Patent 6287,774. Specifically, claim 1 of the instant application is drawn to a method of measuring the activity of a kinase enzyme comprising:

- a) providing a fluorescently labeled phosphorylatable compound, a kinase enzyme and a phosphate donor group where the kinase enzyme transfers the phosphate group from the phosphate donor group to the phosphorylatable compound to make a phosphorylated product,
- b) contacting the phosphorylated product with a protein having a chelating group associated therewith, and a multivalent metal ion chelated by the chelating group, and determining a level of phosphorylated product by detecting a level of fluorescence intensity emitted from the reaction mixture.

Claim 40 of US Patent 6,287,774 is drawn to A method of detecting the phosphorylation of a phosphorylatable compound, comprising:

- a) providing the phosphorylatable compound with a fluorescent label;
- b) contacting the phosphorylatable compound with a kinase enzyme in the presence of a phosphate group in a first mixture;
- c) contacting the first mixture with a second reagent mixture comprising a protein having a chelating group associated therewith, and a metal ion selected from the group consisting of  $\text{Fe}^{3+}$ ,  $\text{Ca}^{2+}$ ,  $\text{Ni}^{2+}$  and  $\text{Zn}^{2+}$ ;
- d) comparing a level of fluorescence polarization from the first mixture in the presence of the second mixture to a level of fluorescence polarization from the phosphorylatable compound with the fluorescent label in the absence of the kinase enzyme.

The claims of the US Patent 6, 287,774 are species of the instant claims.

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5. Claims 1-9 and 17-28 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-15 of copending Application No. 10/397,887. Although the conflicting claims are not identical, they are not patentably distinct from each other because Claim 1 of the instant application is drawn to a method of measuring the activity of a kinase enzyme comprising:

a) providing a fluorescently labeled phosphorylatable compound, a kinase enzyme and a phosphate donor group where the kinase enzyme transfers the phosphate group from the phosphate donor group to the phosphorylatable compound to make a phosphorylated product,

b) contacting the phosphorylated product with a protein having a chelating group associated therewith, and a multivalent metal ion chelated by the chelating group, and determining a level of phosphorylated product by detecting a level of fluorescence intensity emitted from the reaction mixture.

Claim 1 of Application No. 10/397,887 is drawn to a method of determining whether a fluorescently labeled compound is phosphoglated, the method comprising

a) providing a compound in a mixture with a polymer having multivalent cations associated therewith which polymer is sufficiently large to induce a shift in an amount of polarized fluorescence emitted from the mixture when the multivalent metal cations bind the polymer to the compound and

b) monitoring the amount of polarized fluorescence emitted from the mixture to determine whether the multivalent metal cations bind the polymer to the compound such binding being indicative the compound is phosphorylated.

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The claims of Application No. 10/397,887 are a species of the instant claims. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

6. Claims 1-9 and 17-28 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 1 of Application No. 10/855,657. Although the conflicting claims are not identical, they are not patentably distinct from each other because Claim 1 of the instant application is drawn to a method of measuring the activity of a kinase enzyme comprising:

- a) providing a fluorescently labeled phosphorylatable compound, a kinase enzyme and a phosphate donor group where the kinase enzyme transfers the phosphate group from the phosphate donor group to the phosphorylatable compound to make a phosphorylated product,

- b) contacting the phosphorylated product with a protein having a chelating group associated therewith, and a multivalent metal ion chelated by the chelating group, and determining a level of phosphorylated product by detecting a level of fluorescence intensity emitted from the reaction mixture.

Claim 1 of Application No. 10/855,657 is drawn to a method of assaying for kinase activity, comprising:

- a) contacting a fluorescently labeled phosphorylatable peptide substrate with an ATP analog in the presence of a kinase enzyme to yield a first product,

- b) contacting the first product with a reactant that comprises a biotin derivative to yield a second product,



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c) contacting the second product with a biotin-binding protein; and detecting a difference in a fluorescence polarization level from the second product as compared to a fluorescence polarization of the peptide substrate.

The claims of Application No. 10/855,657 are a species of the instant claims. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

7. Claims 1-9 and 17-28 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 1 of Application No. 10/183,040. Although the conflicting claims are not identical, they are not patentably distinct from each other because Claim 1 of the instant application is drawn to a method of measuring the activity of a kinase enzyme comprising:

a) providing a fluorescently labeled phosphorylatable compound, a kinase enzyme and a phosphate donor group where the kinase enzyme transfers the phosphate group from the phosphate donor group to the phosphorylatable compound to make a phosphorylated product,

b) contacting the phosphorylated product with a protein having a chelating group associated therewith, and a multivalent metal ion chelated by the chelating group, and determining a level of phosphorylated product by detecting a level of fluorescence intensity emitted from the reaction mixture.

Claim 1 of Application No. 10/183,040 is drawn to a method of assaying a kinase-mediated coupling reaction comprising:

a) contacting a fluorescently labeled phosphorylatable peptide substrate with an ATP derivative in the presence of a kinase to yield a phosphorylated first product comprising a thiol derivative and the fluorescent label

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b) contacting the first product with a reactant comprising a thiol-reactive derivative and coupling group to yield a second product

c) contacting the second product with a reactant comprising a large molecular weight moiety that specifically recognizes and binds to the coupling group and

d) measuring a difference in the fluorescence polarization level resulting from the second product as compared to the fluorescence polarization of the peptide substrate to determine progress of the kinase-mediated coupling reaction.

The claims of Application No. 10/183,040 are a species of the instant claims. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

### *Claim Interpretation*

8. Claim 1 recites the limitation “contacting the phosphorylated product with a protein having a chelating group associated therewith and a multivalent metal ion chelated by the chelating group.” All proteins have metal binding or “chelating” groups. Applicants have not specifically defined a chelating group in the specification, therefore for the purpose of applying art, any protein will meet the limitation of “a protein having a chelating group associated therewith.”

### *Claim Rejections - 35 USC § 102*

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

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(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4, 7-9, 17-21, 24 and 26-28 are rejected under 35 U.S.C. 102(a) as being clearly anticipated by Coffin et al., (*Analytical Biochemistry*, 02/15/2000).

With regard to claims 1 and 17, Coffin et al. teach measuring the activity of kinase enzyme comprising:

a) providing a fluorescently labeled phosphorylatable compound, a kinase enzyme and a phosphate donor group where the kinase enzyme transfers the phosphate group from the phosphate donor group to the phosphorylatable compound to make a phosphorylated product (see p. 208 col. 1, 2<sup>nd</sup> paragraph),

b) contacting the phosphorylated product with a protein having a chelating group associated therewith, and a multivalent metal ion chelated by the chelating group, and determining a level of phosphorylated product by detecting a level of fluorescence intensity emitted from the reaction mixture (see p. 208, col. 1, 2<sup>nd</sup> paragraph).

With regard to claims 2 and 19, Coffin et al. teach serine, tyrosine or threonine as a substrate (see p. 207 col. 2 paragraph 3 line 3).

With regard to claims 3 and 20, Coffin et al. teach the multivalent metal cations bind the molecule to the phosphorylated product partially due to charge difference between the phosphorylated product and the multivalent metal cation (see p. 211 paragraph 2 lines 9-14).

With regard to claims 4 and 21, Coffin et al. teach the multivalent metal cations bind the molecule to the phosphorylated product partially due to specific binding affinity between the phosphorylated product and the multivalent metal cation (see p. 209 col. 1 paragraph 1).

With regard to claim 7, Coffin et al. teach introducing at least a first test compound to the reaction mixture and comparing the level of fluorescent intensity emitted from the reaction

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mixture in the presence of the test compound to the level of fluorescent intensity emitted from the reaction in the absence of the test compound (see p. 208 col. 1, 2<sup>nd</sup> paragraph).

With regard to claim 8, Coffin et al. teach repeating the steps of introducing and comparing with a plurality of different test compounds (see p. 208 col. 1, 2<sup>nd</sup> paragraph).

With regard to claim 9, Coffin et al. teach the molecule comprises a polymer (see p. 208 col. 2 line 10).

With regard to claim 18, Coffin et al. teach the enzyme modifying the chemical structure of the substrate by addition to, subtraction from, or alteration of its chemical structure (p. 208 col. 1, 1<sup>st</sup> paragraph).

With regard to claim 24, Coffin et al. teach the substrate as phosphorylated and the enzyme is a phosphatase enzyme (see p. 212 col. 1, 3<sup>rd</sup> paragraph).

With regard to claim 26, Coffin et al. teach the substrate includes a substrate for one of a sulfatase, a phosphorylase, an esterase, a hydrolase, an oxidase or an analog thereof (see p. 212 col. 1, 3<sup>rd</sup> paragraph).

With regard to claim 27, Coffin et al. teach using fluorescence polarization detection (see p. 207 col. 1, 1<sup>st</sup> paragraph).

With regard to claim 28, Coffin et al. teach fluorescence intensity detection (see p. 207 col. 1, 1<sup>st</sup> paragraph).

10. Claims 1-9, 17-24, 26 and 28 are rejected under 35 U.S.C. 102(b) as being anticipated by Mallia (U.S. Patent No. 5,527,688; cited in the IDS), as evidenced by Hawley's Condensed Chemical Dictionary (page 236, 237, 12<sup>th</sup> Edition, Van Nostrand Reinhold, New York, 1993) and Whatman Product Guide (pages 65, 66, 1995).

With regard to claims 1 and 17, Mallia teaches measuring the activity of kinase enzyme comprising:

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a) providing a fluorescently labeled phosphorylatable compound, a kinase enzyme and a phosphate donor group where the kinase enzyme transfers the phosphate group from the phosphate donor group to the phosphorylatable compound to make a phosphorylated product (see col. 2, lines 11-21; col. 3, lines 13-16 and 26-47; col. 6, lines 17-31) and a ferric ion paper having  $\text{Fe}^{3+}$  cations bound to it, where the cations bind the paper to the phosphorylated product (col. 2, lines 21-27; col. 3, lines 18-26; col. 5, lines 43-66; col. 6, lines 1-14). Mallia do not specifically teach a cationic polymer, however, as evidenced by Hawley's Condensed Chemical Dictionary, paper is made from cellulose which is a polymer of glucose (page 236). The Whatman Product Guide (page 66) teaches that the 3MM paper is made from pure cellulose, therefore, since Mallia teaches Whatman 3 MM paper modified with iminodiacetic acid (col. 5, lines 56-61) to which  $\text{Fe}^{3+}$  cations are bound, they inherently teach a polymer having multivalent cations associated with it.

b) contacting the phosphorylated product with a protein having a chelating group associated therewith, and a multivalent metal ion chelated by the chelating group, and determining a level of phosphorylated product by detecting a level of fluorescence intensity emitted from the reaction mixture (col. 2, lines 11-21; col. 3, lines 13-16 and 26-47; col. 6, lines 17-31) and a ferric ion paper having  $\text{Fe}^{3+}$  cations bound to it, where the cations bind the paper to the phosphorylated product (col. 2, lines 21-27; col. 3, lines 18-26; col. 5, lines 43-66; col. 6, lines 1-14). Mallia do not specifically teach a cationic polymer, however, as evidenced by Hawley's Condensed Chemical Dictionary, paper is made from cellulose which is a polymer of glucose (page 236). The Whatman Product Guide (page 66) teaches that the 3MM paper is made from pure cellulose, therefore, since Mallia teaches Whatman 3 MM paper modified with iminodiacetic acid (col. 5, lines 56-61) to which  $\text{Fe}^{3+}$  cations are bound, they inherently teach a polymer having multivalent cations associated with it.

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With regard to claims 2 and 19, Mallia teaches serine, tyrosine or threonine as a substrate (see col. 5, lines 26-33; col. 6, lines 18, 19, where Mallia teaches kemptide which a substrate for protein kinase A and kemptide has an amino acid sequence of LRRASLG, therefore by teaching kemptide Mallia inherently teaches a serine substrate).

With regard to claims 3 and 20, Mallia teaches the multivalent metal cations bind the molecule to the phosphorylated product partially due to charge difference between the phosphorylated product and the multivalent metal cation (see col. 2, lines 11-21; col. 3, lines 13-16 and 26-47; col. 6, lines 17-31) and a ferric ion paper having  $\text{Fe}^{3+}$  cations bound to it, where the cations bind the paper to the phosphorylated product (col. 2, lines 21-27; col. 3, lines 18-26).

With regard to claims 4 and 21, Mallia teaches the multivalent metal cations bind the molecule to the phosphorylated product partially due to specific binding affinity between the phosphorylated product and the multivalent metal cation (see col. 2, lines 11-21; col. 3, lines 13-16 and 26-47; col. 6, lines 17-31) and a ferric ion paper having  $\text{Fe}^{3+}$  cations bound to it, where the cations bind the paper to the phosphorylated product (see col. 2, lines 21-27; col. 3, lines 18-26, where the product is bound to the ferric ion paper due to the specific affinity of the for  $\text{Fe}^{3+}$  the phosphoryl group).

With regard to claims 5, 6, 22 and 23, Mallia teaches the multivalent metal cations are  $\text{Fe}^{3+}$  (see col. 2, lines 21-27; col. 3, lines 18-26; col. 5, lines 43-66; where  $\text{Fe}^{3+}$  are trivalent metal cations).

With regard to claim 7, Mallia teaches introducing at least a first test compound to the reaction mixture and comparing the level of fluorescent intensity emitted from the reaction mixture in the presence of the test compound to the level of fluorescent intensity emitted from the reaction in the absence of the test compound (see col. 2, lines 11-27).

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With regard to claim 8, Mallia teaches repeating the steps of introducing and comparing with a plurality of different test compounds (see col. 2, lines 21-27, and Figures 3, 4 and Example 4, where a plurality of samples were compared to make a standard curve).

With regard to claim 9, Mallia teaches Whatman 3MM paper (col. 2, lines 21-27; col. 3, lines 18-26; col. 5, lines 43-66; col. 6, lines 1-14). The Whatman Product Guide (page 66) teaches that the 3MM paper is made from pure cellulose. As evidenced by Hawley's Condensed Chemical Dictionary, paper is made from cellulose which is a polymer of glucose (page 236), therefore by teaching Whatman 3MM paper Mallia inherently teaches a polymer.

With regard to claim 18, Mallia teaches the enzyme modifying the chemical structure of the substrate by addition to, subtraction from, or alteration of its chemical structure (see col. 3 lines 13-26, where Mallia teach a peptide substrate which is phosphorylated by a protein kinase, which adds a phosphate the substrate).

With regard to claim 24, Mallia teaches the substrate as phosphorylated and the enzyme is a phosphatase enzyme (see col. 3 lines 13-26, where Mallia teach a peptide substrate which is phosphorylated by a protein kinase, which phosphorylates the substrate).

With regard to claim 25, Mallia teaches the substrate comprises amino or keto containing substrate and the enzyme comprises an amino transferase (see p. 212, col. 1 paragraph 3).

With regard to claim 26, Mallia teaches the substrate includes a substrate for one of a sulfatase, a phosphorylase, an esterase, a hydrolase, an oxidase or an analog thereof (see col. 3 lines 13-26, where Mallia teach a peptide substrate which is phosphorylated by a protein kinase, which phosphorylates the substrate).

With regard to claim 28, Mallia teaches fluorescence intensity detection (see col. 2, lines 11-27).

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11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claim 25 is rejected under 35 U.S.C. 103(a) as being unpatentable over Mallia (U.S. Patent No. 5,527,688; cited in the IDS), as evidenced by Hawley's Condensed Chemical Dictionary (page 236, 237, 12<sup>th</sup> Edition, Van Nostrand Reinhold, New York, 1993) and Whatman Product Guide (pages 65, 66, 1995) in view of Meade et al. (USPN 6,713,045 B1).

The teachings of Mallia are described previously.

Mallia does not teach amino transferases.

Meade et al. teach a method of detecting target enzymes, specifically Aspartate amino transferase (see col. 14 line65-66).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to use the kinase assays of Mallia to detect the phosphorylation status of an amino transferase as taught by Meade et al. The motivation to do so, provided by Meade et al., is that detecting Aspartate amino transferase is preferred as these enzymes are indicators for treatment of heart disease (col. 14, lines 63-66). An ordinary practitioner would have been motivated to use the kinases assays of Mallia to detect the phosphorylation status of an amino transferase as taught by Meade et al. because phosphorylation and dephosphorylation events are involved in so many cell functions and diseases and amino transfersases can be used as indicators for treatment of diseases, particularly heart disease as disclosed by Meade et al.

### *Response to Arguments*



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12. Applicant's arguments with respect to the Written Description rejections have been considered but are moot in view of applicants amendment filed June 12, 2006.

*Summary*

13. No claims allowed.

*Correspondence*

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Heather G. Calamita whose telephone number is 571.272.2876 and whose e-mail address is heather.calamita@uspto.gov. However, the office cannot guarantee security through the e-mail system nor should official papers be transmitted through this route. The examiner can normally be reached on Monday through Thursday, 7:00 AM to 5:30 PM.

If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Gary Benzion can be reached at 571.272.0782.

Papers related to this application may be faxed to Group 1637 via the PTO Fax Center using the fax number 571.273.8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to 571.272.0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. For more information about the PAIR system, see <http://pair-direct.uspto.gov>.

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hgc

TERESA E. STRZELECKA, PH.D.  
PRIMARY EXAMINER

*Teresa Strzelecka*

*8/18/2006*